DETAILED ACTION

Claims 1 and 6-11 remain under examination.

Withdrawal of Rejections

The rejections not explicitly restated below are withdrawn due to Applicant's response in the amendment filed 6/17/2009.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 6 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuji et al. (WO 02/097107; cited in the IDS filed 6/6/06) in view Suzaki et al (1983; cited in the IDS filed 12/2/08), Kim et al. (2002) and Nilsson (US 6,077,695).

The claims are directed to a method of producing an alpha-1-4-glucan that can be amylose comprising reacting in a solution cellobiose, a primer, a source of phosphate such as inorganic phosphate, cellobiose phosphorylase and an alpha1,4-glucan phosphorylase wherein the byproduct glucose is removed simultaneously from the reaction solution. The reaction solution can further contains glucose isomerase or glucose oxidase. The reaction solution can contain glucose oxidase, mutarotase and catalase. The concentration of the source of phosphoric acid is 1 to 50 mM.

Fuji discloses a method for producing glucans comprising the steps of allowing a reaction solution containing sucrose, a primer, inorganic phosphate (instant claim 9) or

glucose-1-phosphate (G1P), sucrose phosphorylase (SP) and alpha1,4-glucan phosphorylase (GP) to react to produce chain extended glucans such as starch (amylose (p. 14, line 9, instant claim 11); see abstract, p. 13, lines 25-32 and claim 1; instant claim 1, in part). It is noted that this is a coupled reaction in one-pot with all enzymes and reactants present in the same solution (p. 63, lined 4-23). The preferred concentration of the phosphate sources is 20-250mM (lines 8-13, page 38 of the description). This range overlaps the claimed ranged of 1 mM to 50 mM of instant claim 10.

Fuji does not teach that that as cellobiose is used instead of sucrose as the raw material for producing the intermediate G1P (instant claim 1). Nor does Fuji disclose that cellobiose phosphorylase is applied on cellobiose instead of sucrose phosphorylase on sucrose to produce G1P (instant claim 1). Fuji does not teach that the glucose byproduct is simultaneously removed from the solution by reaction with glucose isomerase or glucose oxidase (instant claims 1 and 6).

Suzaki discloses that an alpha-1,4-glucan can be prepared by separate conversion of cellulase to cellobiose, cellobiose to glucose-1-phosphate and G1P to the alpha-1,4-glucan. Starch (amylose, as in instant claim 10) is produced since the final product gives a positive test for iodine staining and the product is completely degraded by glucoamylase, page 65, right column, first paragraph). CBP converts cellobiose to G1P and glucose. The conversion of G1P to amylose occurs with an alpha-1,4,glucan phosphorylase and primer.

Kim teaches that CBP converts inorganic phosphate and cellobiose to glucose ad G1P. Glucose, a product of the reaction is an inhibitor of CBP (page 200, left column, second paragraph under "Reaction mechanism of CBP").

Nilsson discloses a process for producing Glcβ-4GlcNAc derivatives by a transglycosylation reaction that can employ cellobiose as the glucosyl donor (col. 2, lines 20-34). Nilsson teaches that if high concentrations of cellobiose are used, considerable amounts of glucose as a byproduct of the reaction will be formed. The formed glucose will compete with the acceptor and water for the glucosyl-enzyme intermediate, thus inhibiting the synthesis of the product. A second enzyme such as an isomerase or an oxidase can be used to remove the inhibitory glucose during the reaction to improve product yield (col. 7, lines 54-68).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute cellobiose and CBP for sucrose and SP, respectively, to produce G1P which is then used to produce a chain extended alpha-1,4-glucan such as amylose in a coupled reaction system. The ordinary artisan would have been motivated to do so since CBP and SP are both phosphorylases that produce G1P from their respective substrates. Hence, using cellobiose and a cellobiose-processing enzyme is simply an obvious substitution to the same intermediate product G1P and the ultimate end product, starch (e.g., amylose). According to the MPEP 2143:

> B. Simple Substitution of One Known Element for Another To Obtain Predictable Results
>
> To reject a claim based on this rationale, Office personnel must resolve the Graham factual inquiries. Then, Office personnel must articulate the following:

(1) a finding that the prior art contained a device (method, product, etc.) which differed from the claimed device by the substitution of some components (step, element, etc.) with other components;

(2) a finding that the substituted components and their functions were known in the art;

(3) a finding that one of ordinary skill in the art could have substituted one known element for another, and the results of the substitution would have been predictable; and

(4) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.

The rationale to support a conclusion that the claim would have been obvious is that the substitution of one known element for another yields predictable results to one of ordinary skill in the art. If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art.

In the instant case, the combination of sucrose and SP, and cellobiose and CBP serve the same purpose which is produce G1P for further reaction. Hence, the substitution is no more than the predictable use of prior art elements according to their established functions resulting in the simple substitution of one known element for another for a predictable result. The ordinary artisan would have had a reasonable expectation that cellobiose and CPB could be substituted for sucrose and SP, respectively since Suzaki teaches that CPB converts cellobiose into G1P and glucose. The ordinary artisan would have had a reasonable expectation that cellobiose and CBP could be substituted for sucrose and SP, respectively, in a coupled reaction with and α-1-4-glucan phosphorylase in a one pot reaction because sucrose and SP are able to

function in the same reaction system as α-1-4-glucan phosphorylase to ultimately produce chain-extended amylose from G1P, the intermediate product.

It would have been obvious to one of ordinary skill at the time the invention was made to remove the glucose byproduct during the reaction of cellobiose and Pi with CBP to make glucose and G1P wherein G1P is then used to extend an amylose chain by the action of an alpha1-4 glucan phosphorylase. The ordinary artisan would have been motivated to do so in order to prevent glucose from inhibiting CBP, thereby decreasing the yield of the ultimately desired product, chain extended amylose. The ordinary artisan would have been motivated to employ glucose isomerase or glucose oxidase since it is desired to convert glucose into a product that does not inhibit CBP. The ordinary artisan would have had a reasonable expectation that glucose isomerase could successfully prevent glucose from inhibiting CBP by converting the glucose byproduct into a non-inhibitory product (that does not inhbit CBP) because Nilsson teaches that an isomerase or an oxidase is successful in removing glucose byproduct in a similar enzymatic reaction, thus preventing product inhibition.

Claims 1-4 and 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuji et al. (WO 02/097107; cited in the IDS filed 6/6/06) in view of Suzaki et al. (1983; cited in the IDS filed 12/2/08), Kim et al. (2002), Wada et al. (JP 2003093090; machine translation) and Taguchi et al. (1994, abstract only).

The combined disclosures by Fuji and Suzaki are discussed supra.

The combined disclosures do not teach that the glucose byproduct is removed from the solution by reaction by simultaneous reaction with glucose oxidase, mutarotase and catalase (instant claims 6-8).

Kim teaches that CBP converts inorganic phosphate and cellobiose to glucose ad G1P. Glucose, a product of the reaction is an inhibitor of CBP (page 200. left column, second paragraph under "Reaction mechanism of CBP").

Wada teaches that it is desirable to remove glucose when it is a byproduct in the enzymatic conversion of sucrose to inulin because it will increase the yield of the desired product, inulin. The glucose byproduct is removed by converting it into another substance in order to increase the yield of a desired product. Glucose oxidase can be used to convert glucose to gluconic acid thus removing glucose and increasing the yield of inulin (sections [0001], [0011] and [0012]).

Taguchi teaches that blood glucose interferes with the enzymic determination of 1,5-anhydroglutiocol by glucose 2-oxidase. The undesired glucose is removed by employing glucose oxidase, mutarotase and catalase to convert the unwanted glucose to a non-interfering product.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a system comprising glucose oxidase, mutarotase and catalase to eliminate the glucose byproduct in a reaction system that converts cellobiose and Pi to G1P and glucose wherein the G1P is used to extend the chain of amylose by the action of alpha 1-4 glucan phosphorylase. The ordinary artisan would

have been motivated to do so because the elimination of glucose would prevent product inhibition of CPB, thus, increasing the yield of the desired product, amylose. The ordinary artisan would have had a reasonable expectation that the trio of enzymes would successfully eliminate unwanted glucose byproduct because Taguchi teach that the combination of glucose oxidase, mutarotase and catalase are successful in removing glucose that interferes with the determination of 1,5-anhydroglutiocol in blood.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN HANLEY whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Sandra Saucier/
Primary Examiner, Art Unit 1651

/Susan Hanley/
Examiner, Art Unit 1651